(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



1 (88) 8 (1) (81) 1 (81) 1 (81) 1 (81) 1 (1) 1 (1) 8 (1) 1 (1) 8 (1) 1 (1) 8 (1) 1 (1) 1 (1) 1 (1) 1 (1) 1 (1)

(43) International Publication Date 10 July 2003 (10.07.2003)

PCT

(10) International Publication Number WO 03/055522 A1

- (51) International Patent Classification⁷: A61K 45/06, 31/40, 31/415, A61P 35/00
- (21) International Application Number: PCT/EP02/13092
- (22) International Filing Date:
 18 December 2002 (18.12.2002)
- (25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 02075052.7

2 January 2002 (02.01.2002) EI

- (71) Applicant (for all designated States except US): PHAR-MACIA ITALIA SPA [IT/IT]; Via Robert Koch 1.2, I-20152 Milan (IT).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): GERONI, Maria, Cristina [IT/IT]; Via Correggio, 48, I-20149 Milan (IT). FOWST, Camilla [IT/IT]; Via Fratelli Zola, 49, I-20153 Milan (IT). COZZI, Paolo [IT/IT]; Via Zanella, 48/5, I-20133 Milan (IT).

- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

 as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations

Published:

- with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMBINED THERAPY AGAINST TUMORS COMPRISING SUBSTITUTED ACRYLOYL DISTAMYCIN DERIVATIVES AND PROTEIN KINASE (SERINE/THREONINE KINASE) INHIBITORS

(57) Abstract: The present invention provides the combined use of acryloyl distamycin derivatives, in particular α -bromo- and α -chloro-acryloyl distamycin derivatives of formula (I), as set forth in the specification, and a protein kinase (serine/threonine and tyrosine kinases) inhibitor, in the treatment of tumors. Also provided is the use of the said combinations in the treatment or prevention of metastasis or in the treatment of tumors by inhibition of angiogenesis.